THE ACCESSORY THYROIDS IN DOGS PARTIALLY DEPRIVED OF THE THYROID GLAND.

Accessory thyroid glands were searched for and found in dogs 9, 11, 101, 113, 114, 118, 306, 318, 230, and 701. The accessory thyroids always presented precisely the same histological picture as the remains of the thyroid gland in the neck.

SUMMARY.

1. One and three-fourths of the dog's thyroid gland may be removed without appreciably affecting the remainder of the gland.
2. In only 3 of the 59 dogs on which the operation of piecemeal removal was performed did the remaining gland change from a normal to a hyperplastic state. Dogs Nos. 9, 11, and 114.
3. In 5 of the 59 dogs the remaining gland reverted from the early hyperplastic state to the normal state. Dogs Nos. 1, 9, 102, 311, and 314.
4. Where a diagnosis of some degree of hyperplasia was made at the first operation, the pieces removed from the same dogs at subsequent operations had not undergone further hyperplasia.
5. Of the pieces removed from 56 dogs at the first operation, 58 per cent. were normal, 32 per cent. showed early glandular hyperplasia, 5 per cent. marked glandular hyperplasia, and 5 per cent. very early glandular hyperplasia.
6. Definite increase in the size of the remaining gland (hypertrophy) was not observed.
7. The remains of the thyroid lobes, the accessory thyroids, and the successful grafts in a given dog, presented the same histological picture.
8. In no dog was myxedema or tetany observed in which as much as one-fourth of the thyroid and one parathyroid gland were preserved.

PITUITARY DISEASE: A CLINICAL STUDY OF THREE CASES.

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The main purpose of this paper is to record and comment upon several cases of pituitary disorder which present noteworthy clinical features. The literature of this complex subject has become so extensive that an attempt to epitomize it cannot be made here.

Much careful clinical observation and animal experimentation is still necessary to solve the hypophysis problem, especially in its interglandular correlations and in its role in the "sex-levelling" process.

Since Marie first directed attention in 1886 to this hidden gland as a factor in disease, it has been subjected to so much scrutiny that it is in danger of becoming overworked as a *causa morbi.* The association of destructive and atrophic lesions of the hypophysis with clinical manifestations is close. The dependence of dystrophia adiposogenitalis—typus Froehlich—on hypopituitarism may be considered as proved. This form, which is characterized by defective development of secondary sexual characteristics, atrophic genitalia, hypotrichosis, and adiposity, has its prototype in animal experimentation. Cushing[1] says: "Our first experience, therefore, with hypophysectomized adult canines deprived of all but a fragment of the pars anterior disclosed a clinical syndrome with adiposy, increased sugar tolerance, lowered body temperature, and reversive sexual changes as its chief features. Later experiences, with the production of corresponding hypophysial defects in puppies, disclosed a similar syndrome, with a persistence of sexual

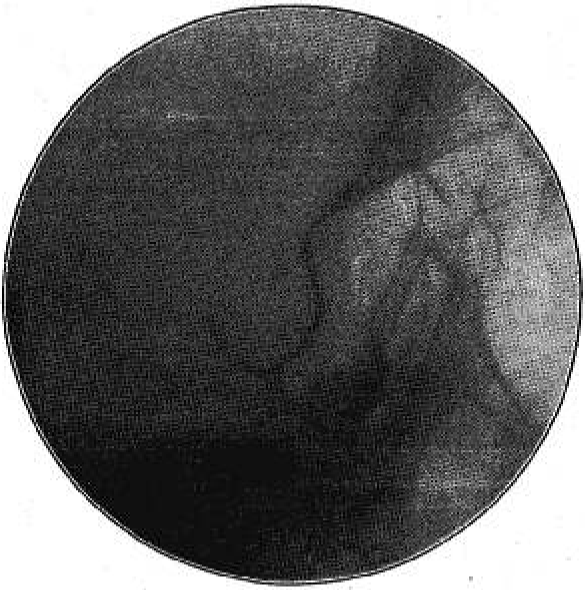

FIG. 1, A. B.—Sella measures 12 x 16 mm., Note thin retroposed and retroverted cantel. The skiagraph was taken from a normal male, aged forty-eight years, who suffered from migraine.

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[1] The Pituitary Body and its Disorders, Philadelphia, 1912.

infantilism and the additional factors of skeletal undergrowth and evident psychical disorders."

The case is different in acromegaly. Although circumstantial evidence for a hyperpituitarism or perverted secretion of the pars anterior as its cause is most conclusive, yet it is not absolute. The operative experience of Hochenegg and Exner in acromegaly approaches the experimental in the definiteness of results.[2]

The case is much the same with gigantism, and as a working hypothesis, we must accept the dictum of Launois and Roy that gigantism is acromegaly in subjects whose epiphyseal cartilages are not ossified no matter what the age.

The sequence of hypophysial struma and disturbed sexual or skeletal development is not invariable. This is shown by one of our cases in which an eroded sella, 12 mm. x 16 mm. (Fig. 1), was found in a medium-sized man, aged forty-eight years. The only possible growth anomaly was delicately shaped hands and fingers. His sexual development and sexual life have been normal. The patient had long been a sufferer from proxysmal headaches, which were relieved after alkalization thoroughly carried out over a period of several years. Such cases must make us accept with reserve sellar deformity and enlargement, *i. e.*, hypophysial struma, as proof of dyspituitarism in seeking for an explanation of clinical facts.

The relationship of the pituitary gland to diabetes mellitus and insipidus will be taken up after the case reports.

Case I.—A. L., aged sixty-one years, came under observation in January, 1908. In August, 1907, after a hard day's work in a cold-storage room he suddenly became weak, dizzy, and faint; a hemoptysis of one pint of bright red blood followed. A second hemorrhage occurred the same evening after he had entered St. Joseph's Hospital. For three weeks he spat blood daily and was much troubled with weakness and drowsiness. An intermission of about two months was followed by another hemorrhage brought on by heavy lifting. He then reëntered the hospital, where he has since remained as an orderly.

During the winter of 1908 he had many attacks of the following description: After a couple of days of malaise, weakness, intense parietal headache, tinnitus aurium, vertigo, palpitation, and of periocular edema a sudden rise in temperature (102° to 104°), with hemoptysis, would occur. At such times an area 4 to 10 cm. in diameter of impaired resonance with fine moist rales could be demonstrated in the lungs. The area was always sharply localized and usually to be found posteriorly in the upper part of one of the lower lobes. With the onset of hemoptysis the edema of the eyelids would rapidly disappear. The hemoptysis and temperature would cease two or three days later. These attacks occurred at frequent intervals for four months, when only an evanescent edema of the eyelids reoccurred at intervals of decreasing frequency. The leukocytes during the attacks varied from 7100 to 9000. A conjunctival tuberculin test and repeated sputum examinations for tubercle bacilli were negative. Repeated physical examinations during the intermissions revealed nothing except a moderate pulmonary emphysema and rapidly enlarging finger tips, which were at first considered to be a osteopulmonary arthropathy. Six months later the marked changes which had taken place in his hands, feet, and face, the increase in weight, the kyphosis, etc., made the clinical diagnosis of acromegaly certain.

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[2] Hochenegg, J., Operativ geheilte Akromegalie bei Hypophysentumor, Verhandl. d. Deutsch. Gesellsch. f. Chir., 1908, vol. xxxvii, pp. 80 to 85; Exner, A., Rückgang der akromegalischen Erscheinungen nach Operation eines Hypophysentumors, Wien. klin. Woch., 1909, vol. xxii, pp. 108 to 109.

At present (January 14, 1914) the patient complains merely of occasional swelling of the eyelids and slight attacks of weakness and drowsiness, which pass quickly on lying down.

Status Præsens. The patient is a large, heavy-set, elderly man (since the onset of his trouble his weight has increased from 140 to 265 pounds), the countenance is conspicuous for its prognathism, prominent cheek bones, squareness, beetling shaggy eyebrows, thick lips, muddy, pasty complexion, and apathetic expression. There is distention of the supra-orbital veins, which becomes evident on exertion or excitement. The palpebral fissures are narrow, the fundi are normal, the teeth are poor, and the tongue is normal in size. The trunk, legs, and arms are massive, the hands and feet are spade-like, the phalanges are thick, heavy, and bulbous. There is a marked increase in subcutaneous fat, and the abdomen is pendulous. There is a well-defined kyphosis of the cervicodorsal spine. There is no adenopathy, no increased area of thymic dulness, and no pigmentation. The thyroid, tonsils, and testicles are small (his sexual potency has always been very low). Perimetric examination reveals contraction, especially of the temporal fields, and a moderate interlacing of the color fields. The sella measures 17 x 11 mm., (Fig. 2). The dorsum epiphii is retroposed and retroverted. The posterior clinoid processes are thickened. The sphenoparietal sinuses with their branches are especially marked. The dentations of the lamboid suture are large and the digital impression are rather better defined than usual.

The patient took 400 grams of levulose at one time without excreting sugar. The most interesting features in this case are the peculiar angioneurotic edema of the periocular structures and the striking pulmonary phenomena. The character of the sputa and the dulness suggested infarct. The absence of cause for infarction and of disturbed general pulmonary circulation pointed rather to either an ephemeral pneumonia or an evanescent, intense, localized hemorrhagic edema of the lungs. Pneumococci were not found in the sputa in any numbers, and the clinical course, observed during repeated attacks, was not that of abortive pneumonia. The best explanation is that it was a process similar to and of the same etiology as the edema of the eyelids, which always preceded or accompanied the lung manifestations. The anatomical lesion must have consisted of *congestion of a sharply localized lung area, with extravasation of blood and serum into the alveoli* extensive enough to impair resonance. Whether the association of the above-described syndrome with hypophysis disease is of any significance must be determined by other observations.

His subnormal sexual life and development as suggestive of a veiled hypopituitarism persisting until his fifty-sixth year is also of interest.

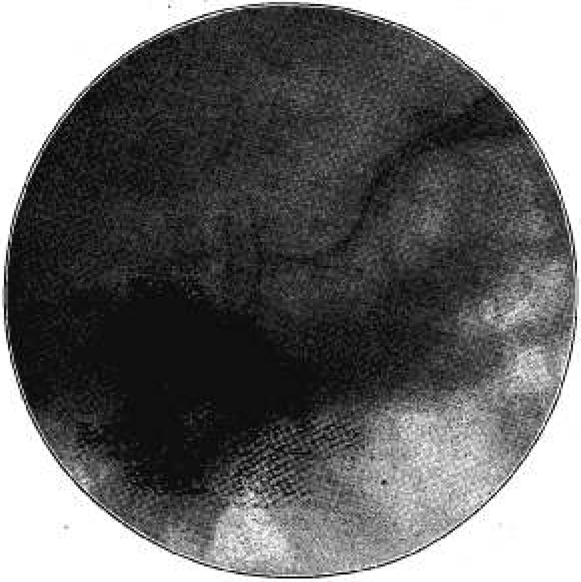

FIG. 2, A. L.—Acromegalic. Sella measures 11 x 17 mm. Note the retroversion, the retroposition, and the thickening of the dorsum epiphii. The sella also appears "dished."

CASE II.—M. V., aged twenty years, consulted me April 4, 1909, for amenorrhea and for *transitory disturbances in her ability to express her thoughts in words*. There had been four such "spells" in the preceding three months. She had suffered an epileptiform attack the preceding day, followed by a dazed state and severe headache. The right arm was limp for a few moments. There was nothing of significance in the family or previous history.

Physical examination showed a large, fat girl with undeveloped breasts; there was no pubic or axillary hair; there was a slight congenital asymmetry of the face; the eye muscles and fundi were normal; the power of the dorsal flexors of the right foot was diminished; the knee- and ankle-jerks were sharper on the right side, and there was a positive Babinski on the same side. There was no adiadokokinesis or Romberg's sign; the abdominal reflexes on the right side were diminished; the uterus was infantile. Otherwise the physical examination showed nothing of significance. A diagnosis of *intracranial neoplasm affecting the hypophysis—typus Froehlich*—was made.

July 30, 1910. The following notes were made: The patient has grown very rapidly during the past year. Nocturnal epilespy has been common. The face was large, the skin coarse, and the expression stupid. The hands and feet were large and long, and the jaw was undershot. There had been a slight development of the pubic hair. The right masseter seemed weaker than the left The examination of the nervous system revealed the same findings as formerly. The patient was put on pituitrin (P. D.) ♏x, t. i. d.

December 1, 1911. The menses have been practically normal since the pituitrin was started. The pubic and axillary hair have developed moderately. Headaches, vomiting, and attacks of unconsciousness have been less than formerly.

September 28, 1912. The following was noted: The patient has only missed two menstrual periods in the last two years. She has become much heavier and more obese. The features have grown coarser and cerebration very slow. She complained of frequent attacks in which she became dazed and everything seemed unreal—*uncinate attacks without olfactory aura.* The acromegalic features were marked. There was a considerable amount of spotted brown pigmentation all over the body, which had appeared since last seen (adrenal insufficiency). There was weakness and slight spasticity of the muscles of the right upper and lower extremities. The tendon reflexes on the right side were all increased; Babinski, Oppenheim, and Gordon reflexes were all present on this side. The abdominal reflexes on the right side were gone. The facial muscles were distinctly weaker on the right side; the fundi were normal; perimetric examination showed interlacing of the color fields and contractions of all of the fields, especially on the temporal side; 150 grams of levulose, 350 grams of levulose, and 400 grams of glucose were given on different days and the urine collected; there was no glycosuria.

The sella measures 13 x 15 mm. (Fig. 3). The triangular excavation into the sphenoidal cells is noteworthy. The digital impressions were specially well marked in this case. The unusual shape of the sella and the secretory phenomena would lead one to suspect an infiltrating growth arising from the hypophysis, although the focal symptoms would point rather to an *interpeduncular growth which interfered with the infundibulum and consequently* *with the cerebrospinal fluid.* The osseous overgrowth associated *with increase* in carbohydrate tolerance is significant, inasmuch as diminution in carbohydrate tolerance has been frequently noted in hyperpituitarism.[3] The transition of a hypopituitarism of the Froehlich type into a hyperpituitarism resulting in acromegaly is striking—hyperactivity of the anterior lobe with deficiency of the posterior lobe—and demonstrates the clinical existence of disassociation of the anterior and posterior lobes.

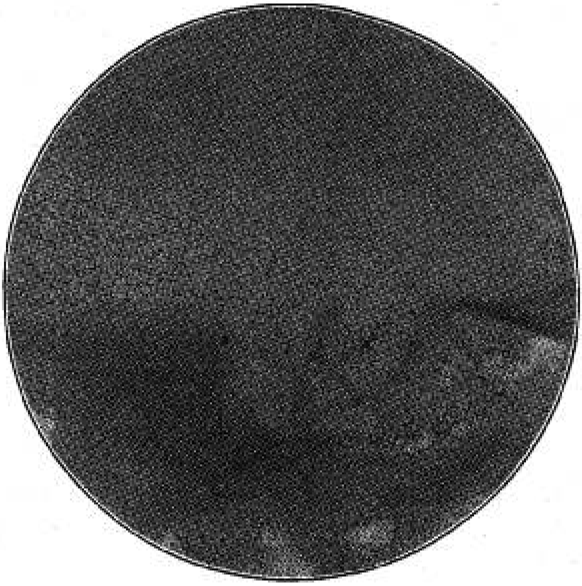

FIG. 3, M. V.—Sella measures 13 x 15 mm. Note the peculiar pyramidal shape which suggests erosion of the floor by an infiltrating process.

CASE III.—Mrs. N. was referred to me by Dr. Dierker, of Lawrence, September 1, 1913. She is twenty-three years old, has been married four years, has borne two healthy children, and has had no miscarriages. The family and past histories were negative. The present complaint began one year ago, four months after parturition. The onset was gradual, and the first thing noticed was that she was inclined to mope in a corner and show marked mental sluggishness.

The patient complained only of tiring easily and of attacks of dizziness, weakness, and depression, which come on suddenly. During the past year she has gained forty pounds, and a marked change has taken place in her facial contour. There has been no gastro-intestinal, genito-urinary, or cardiovascular disturbances. She has suffered occasionally from occipital headaches.

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[3] Cushing, loc. cit.; Ravault, Bull. et mém. Soc. méd. d. hôp. de Paris, 1900, vol., xvii, pp. 352 to 360; Borchardt, L., Funktion u. funtionelle Erkankungen der Hypophyse, Ergebnisse der innere Medizin u. Kinderheilkunde, 1910, vol. iii; Leri André, Akromegalie, innere Sekretion u. Nervensystem, Berlin, 1913, pp. 281 to 313.

The menses began at the age of fourteen years, and have always been normal. She married at the age of nineteen, and her husband states she was sexually undeveloped, and that there was no intercourse during the first year of marriage.

The patient was a large, dull, heavy-set, obese, apathetic young woman; she took little interest in her surroundings, and was unreasonable and inclined to be peevish and unruly; she would laugh or cry by the hour or sit as if in a trance. One day she spent two hours looking out of the window without changing position. Her face was square, the supra-orbital ridges were prominent, and the cheek bones protruded rather conspicuously; the face was flattened and heavy, but there was no special prognathism; the tongue was not thickened. The body was massive; the subcutaneous fat was abundant; there was a moderate growth of genital and axillary hair, with quite a little hair scattered along the linea alba. Examination of the heart, arteries, abdomen, and reflexes revealed nothing abnormal; there were no sensory disturbances; the urine was normal, although the daily output was only 400 to 600 c.c. Satisfactory perimetric observations could not be made.

The following tests to determine the carbohydrate tolerance were made: 150 grams of glucose were given in tea; on the second day 300 grams of glucose were given in tea; on the third day 450 grams were given in lemonade. After each administration the urine was collected for eight hours. In none of the tests was a reducing substance found. Marked diminution of urine was noted while these tests were in progress.

The sella measured 10 x 13 mm. (Fig. 4). There is some retroversion of the cantel, and the posterior clinoid processes seem thickened.

Fifteen minims of pituitrin (P. D.) were given hypodermically A.M. and P.M. This resulted in considerable loss of weight and a notable improvement in her mental condition.

The sexual history of the patient is important. The possibility of an antecedent hypopituitarism, manifested by complete absence of libido, with normal procreative functions, is of interest. Sexual intercourse was granted only at rare intervals, and then under protest. The lack of interest in husband, home, children, and in her wifely duties in general was significant. The husband believed her mentally unsound, and desired that she be committed; therefore the case assumes a medicolegal aspect. A report received February 4, 1914, states that she has lost about twenty pounds in weight and that she has become more active sexually. She has taken Armour's desiccated pituitary gland tablets in an irregular and desultory fashion.

The mental hebetude, lack of initiative, psychical depression, and negativism in this case strongly suggested the hebephrenic type of dementia precox. The increased sugar tolerance, osseous changes, physiognomy, and the clinical course spoke for pituitary disorder. It would seem well to bear in mind the possibility of pituitary disease in suspected cases of dementia precox corresponding to the above-described patient. Likewise the class of cases commonly designated as "fat anemics" should be analyzed with a possible pituitary disturbance in view. This condition commonly affects women about the menopause, and is characterized by increased fat, secondary anemia, and the whole train of neurotic symptoms. The treatment of these cases is highly unsatisfactory, as they react little to the ordinary therapeutic measures. One of these women upon whom operations, rest cure, forced feeding, suggestion, corpus luteum, etc., had been tried, improved markedly on pituitrin. Her sella measured 10 x 13 mm., and her physiognomy strongly suggested acromegaly (this change developed markedly while under observation).

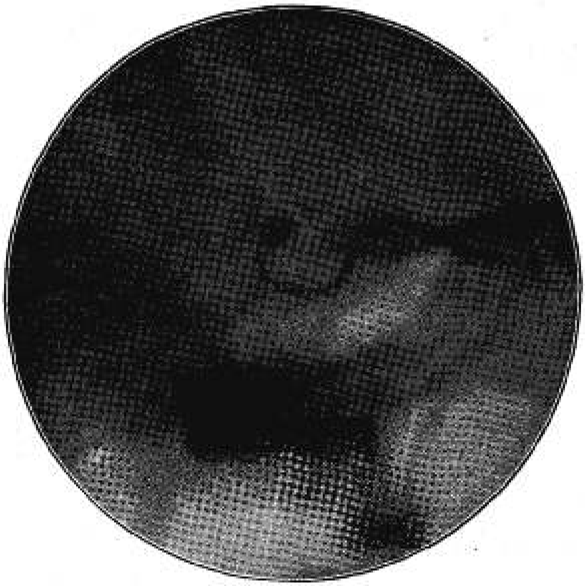

Fig. 4.—Sella measures 10 x 13 mm. The dorsum epiphii appears thickened. Acromegalic symptoms are developing rapidly in this case, although the sella is not markedly changed.

The scope of this paper does not permit of a systematic treatment of the symptomatology of pituitary disorder, and we wish merely to consider briefly the sellar phenomena and certain secretory disturbances.

The roentgenological skull findings in hypophysis disease are manifold and often difficult of interpretation. Sellar enlargement does not necessarily mean *clinical* hypophysis disease, nor does an extremely small sella mean hypopituitarism; therefore much care must be exercised in the interpretation of sellar changes.

The following types may be considered:

1. *Intrasellar growths* widen and deepen the sella so that its floor approaches the floor of the middle fossa. The dorsum epiphii is thinned out, shoved backward, tipped backward, and elongated. Often the posterior clinoid processes partake of the general osseous overgrowth in acromegalics. Changes elsewhere in the skull are often demonstrable—namely, prognathism, large sphenoidal, frontal, and superior maxillary sinuses, thickened skulls, widened sphenoparietal sinuses, digital impressions, and broad sutures with excessive suture indentations.

2. *Extrasellar growths* tend to produce dishing.[4] The cantel is widened, thinned, and shortened; the floor maintains its normal relation to the base of the skull; acromegalic changes, as a rule, are absent, and there is rather thinning than thickening of the skull.

3. *Large hypophysis tumors* may give rise to complete destruction of the sella, often invade the sphenoidal sinuses, and rarely they may completely destroy the body of the sphenoid. Their extra- or intrasellar origin often cannot be determined at this stage. The anterior clinoid processes may point to their origin, *i. e.*, they are often pushed upward and elongated in intrasellar growths while they are shortened in extrasellar growths.

4. Processes which give rise to increased intracranial pressure will frequently produce changes in the sella. They are more inclined to affect the sella asymmetrically; occasionally basal tumors will distort the sella in such manner that roentgenological differentiation is impossible. Tumors arising in the sphenoid itself may even destroy the surrounding structures and leave the sella more or less intact.[5]

The value of good plates in obscure disorders of growth and of sexual development and activity, and in symptoms pointing to intracranial mischief, can hardly be overestimated. Disturbances of vision, migraine, epileptic attacks, psychical anomalies, trophic disorders—such as obesity, infantilism, impotence, gigantism, dwarfism, menstrual disturbances, without pelvic explanation—should call for an *x*-ray examination. We have been able to watch the development of pituitary disorder in two epileptics in whom the plates showed sellar deformation. Cushing's case of migraine, which was completely relieved by sellar decompression, is worthy of note in this connection.

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[4] Schüller, Artur, Roentgen-Diagnostik der Erkrankungen des Kopfes, Wien. u. Leipzig, 1912.

[5] Schüller, loc. cit.

Recently much evidence has been brought forward to prove the association of diabetes insipidus with pituitary disease. Frank[6] goes so far as to maintain that all diabetes insipidus is due to posterior lobe hyperactivity. Hypophysectomized animals excrete several times the normal amount of urine in the days following operation.[7] The same fact has been observed in operated cases. Often glycosuria is present in the first days, to be followed later by an increased sugar tolerance.[8] This is in keeping with the fact that acromegalics often show decreased sugar tolerance during the developmental stage and later show increased tolerance. Goetsch, Cushing, and Jacobson found in their experiments on carbohydrate metabolism following partial hypophysectomy that there was a transient glycosuria followed by increased carbohydrate tolerance, which could be reduced below the normal by the administration of posterior lobe extracts. A remarkable case has recently been reported by Simmonds[9] in which a diabetes insipidus followed a carcinomatous metastasis into the pars posterior in which the normal structure was almost entirely destroyed. The pars intermedia and pars anterior were intact. In two cases of diabetes insipidus observed by us the sugar tolerance was high; 450 grams of glucose were given at one time without the appearance of sugar in the urine. The curious fact was observed that *while taking the large amount of sugar the quantity of urine was markedly diminished.* Sellar changes were present in three cases of diabetes insipidus studied, either as enlargement, deformation, or erosion.

The following nosological schema, although not comprehensive, will serve to sketch the conditions resulting from the failure of the pituitary gland to discharge its particular functions in the interlocking glandular directorate which controls metabolism, growth, and sexual life:

1. Affections of the pars anterior:
   (*a*) Hyperfunction—acromegaly, gigantism.
   (*b*) Hypofunction—true or pituitary dwarfism (not chondrodystrophic, rachitic, or cretinic dwarfs).
2. Affections of the pars posterior:
   (*a*) Hyperfunction—diabetes insipidus.
   (*b*) Hypofunction—hypophysial obesity (dystrophia adiposogenitalis).

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[6] Ueber Beziehungen der Hypophyse Zum Diabetes Insipidus, Berl. klin. Woch., 1912, p. 392.

[7] Crowe, Cushing, Homans, Quart. Jour. Exper. Physiol., vol. ii, pp. 389 to 400.

[8] Goetsch, Cushing, and Jacobson, Carbohydrate Tolerance and the Posterior Lobe of the Hypophysis Cerebri, Bull. Johns Hopkins Hosp., 1911, vol. xxii, pp. 165 to 190.

[9] Münch. med. Woch., No. 60, pp. 127 and 128.

3. Mixed affections:
    - (*a*) Hyperfunction of the pars anterior with hypofunction of of pars posterior—acromegaly with hypophysial obesity.
    - (*b*) Hypofunction of both lobes—dwarfism with hypophysial obesity.

4. Hypophysial disturbance, in conjunction with perverted activity of other glands.
    - (*A*) Ovarian or testicular hypofunction with:
        - I. Hyperfunction of pars anterior—acromegaly with sexual impotence—eunuchoid giants.
        - II. Hypofunction of the pars anterior—pituitary dwarfism with sexual impotency.
        - III. Hypofunction of pars posterior—dystrophia adiposogenitalis—genital obesity.
    - (*B*) Associated with disturbances in the functions of other ductless glands, *i. e.*, adrenals, pancreas, thyroid, pineal gland, thymus (status thymolymphaticus), etc.

MENTAL MANIFESTATIONS IN TUMORS OF THE BRAIN.

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A review of the literature concerning mental disturbances in cases of tumor of the brain shows that it is impossible in the light of present knowledge to determine with any degree of accuracy in what particular tumor a certain group of mental manifestations will occur, neither is it possible to draw definite inferences from the seat of the tumor. The literature on this subject is abundant. Classifications have been attempted and tables drawn up to show the frequency of mental disturbances in tumors of various localities of the cerebrum, but a close analysis reveals contradictory statements from equally competent authors.

Some writers believe that in the majority of cases of tumors of the brain disturbances of intellect are observed. They vary from simple intellectual sluggishness to global dementia. The following manifestations are most frequently observed. A stuporous state predominates in the majority of cases. Whether it is exclusively under the influence of the severe pain in the head or it is independent of the latter it is not always easy to interpret. A state of somnolence is quite usual. Indifference and apathy are common. The patient shows lack or loss of interest in surroundings. An intellectual